Pharmacology Rounds

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• Nothing to disclose

#1) Topical Antibiotics

Fourth Generation Fluoroquinolones

• Gatifloxacin .5% (Zymaxid)
• Moxifloxacin .5% (Vigamox)
• Moxeza
• Besivance
• ? Quixin

Fourth generations

• Second generation fluoroquinolones bind only to topoisomerase 4 or DNA gyrase, 4th generations bind to both. Therefore not one but two genetic mutations are required for resistance.
• This has certainly helped, but as always, the bugs are figuring it out
• Pediatric use generally down to one year and older

ARMOR (antibiotic resistance monitoring in ocular microrg.) study

• Studied 592 ocular isolates
• 200 staph aureus, 144 coagulase negative staph, 75 strep pneumoniae, 73 haemophilus, and 100 pseudomonus
• All susceptibility studies were performed at the same lab
ARMOR study
- 39% of staph aureus was MRSA
- 80% of MRSA exhibited Fluoroquinolone resistance
- Besivance proved to show the least resistance across isolates
- Resistance was shown to be a significant problem with multiple drugs and multiple bugs. Ongoing follow up data, now on 3237 isolates, continues to support these original findings, with resistance continuing to worsen in some, but improve in others. MRSA actually stayed the same

Gatifloxacin
- Zymaxid .5%
- Excellent, broad spectrum agent
- TID for bacterial conjunctivitis
- Original was Zymar, discontinued

Moxifloxacin
- Vigamox .5%
- Excellent broad spectrum agent
- Preservative free
- TID dosing for conjunctivitis
- Moxeza .5%
- Different vehicle, and preserved
- Longer contact time, so BID conjunctivitis dosing
- Pediatric use at 4 months and older

Besivance
- Besifloxacin .6%
- Excellent, broad spectrum agent
- Need to shake
- No oral version, so less problems with resistance

Quixin
- .5% concentration of levofloxacin
- ? 4th generation
- Iquix: 1.5%, has been discontinued.

Older Fluoroquinolones
- Ciloxan
- Ocuflox
Ciloxan
- .3% Ciprofloxacin, generic available
- Second Generation
- Good gram-negative coverage, adequate pos.
- Weak against Strep, great against Pseudomonas
- White precipitate often seen in bed of ulcer with treatment. Occurs 15% of the time, increases dramatically with age (pH based)
- Has an available ointment

Ocuflox
- .3% Ofloxacin: generic
- Second generation
- Good gram-negative, better pos.
- Less effective against Pseudomonas
- Much better tissue penetration than Ciloxan...present in therapeutic levels in the AC
- Often used as inexpensive but effective prophylaxis with cataract surgery

Aminoglycosides
- Tobramycin
- Gentamycin
- Neomycin
- All work by inhibiting bacterial protein synthesis. Are bactericidal
- Highly effective against gram-negative bacteria, especially Pseudomonas
- Effective against gram-positive bacteria but less so with ever increasing resistance

Aminoglycosides
- Side effects common to the entire class include PEK (epithelial toxicity), potential allergic reactions, and eyelid edema / erythema
- Cost effective due to generic availability (4$ plans)

Tobramycin .3%
- Available generically in drop and ointment form. Ointment is very expensive!
- More effective and less toxic than Gentamycin
- Less allergic potential than Neomycin
- Tobradex (Tobramycin & Dexamethasone)
- Tobradex ST: lower concentration of dexamethasone (.05%)
- ZyLet (Tobramycin & Loteprednol)
- Pediatric use 2 months and up

Gentamycin .3%
- Available generically in drop and ointment form
- Overall, slightly less effective and slightly more toxic than Tobramycin
- Less allergic potential than Neomycin
- With the arrival of generic Tobramycin, Gentamycin’s use dropped off considerably
- Not rated for pediatric use
Neomycin

- Not available as a stand alone drug
- Ointment or drops in combination with other medications. Highest potential for allergy
- Neosporin drops (Neomycin, Polymyxin, Gramacidin)
- Neosporin Ointment (Neomycin, Polymixin, Bacitracin)
- Maxitrol / Dexacidin (Neo / Poly / Dxa)

Others

- Polytrim
- Erythromycin
- Bacitracin
- Sulfacetamide 10%
- Azasite

Polytrim

- Polymyxin-B and Trimethoprim
- Polymyxin great against gram negative, destroys cell membranes
- Trimethoprim inhibits folic acid synthesis and creates bacteriostasis. Effective against gram-positive and gram-negative except Pseudomonas

Polytrim

- Excellent choice in pediatric infections. 2 months and up
- Very effective against Haemophilus and Streptococcus pneumonia which are the most common causes of childhood eye infections.
- Drop form only-generic available
- Good against MRSA (LASIK in susceptible populations)

Erythromycin

- .5% ointment only (Ilotycin)
- Bacteriostatic-inhibits protein synthesis
- Good gram-positive, marginal gram-negative
- Not good for active therapy, supportive only
- Prophylaxis for ophthalmia neonatorum, though pediatric rated at 2 months and above

Bacitracin

- Ointment only
- Degrades cell walls......works on gram positive only
- Great against Staph so good choice for blepharitis treatment
- Polysporin ointment (Bacitracin and Polymixin). Good gram pos. and good gram negative from polymyxin
Sulfacetamide 10%

- What's old is new again....
- Many of today's bacterial strains have never been exposed
- Resistance is currently actually low
- High allergy rate

AzaSite

- 1% Azithromycin in Durasite vehicle
- Approved for bacterial conjunctivitis: Used for MGD too, AIC
- Bacteriostatic, not bactericidal
- Conjunctivitis dosing is BID for two days, QD for five days so nine drops total for treatment course
- Very expensive, especially considering the fact that only nine drops are used
- May already be facing considerable resistance due to long time systemic use. Pediatric rated at one year and up

#2) Topical Steroids

Quick review of topical steroids

- Several topical steroids available for ocular use
- Long track records for many of them with proven efficacy
- Differing levels of activity with differing side effect profiles
- Various clinical niches for different drugs
- Side effects well known.......PSC’s (< orals), increased IOP (> orals), etc.

Prednisolone Acetate

- Most commonly used topical steroid
- Potent “gold standard” with good mix of effectivity and side effect profile
- .12% suspension (Pred mild)
- 1% suspension (Pred Forte, Omnipred). Econopred no longer exists: replaced by generic Omnipred with smaller molecule.

Prednisolone phosphate

- Goes on and off the market in generic form
- Rarely used
- Vasocidin drops in combo with Sulfacetamide
- Used in the SCUT trial
Durezol

- 0.05% Ophthalmic emulsion
- ½ dosing schedule compared to Pred Forte and others
- Expensive!
- Very effective against iritis, can be drug of choice
- Very high propensity to elevate IOP

Loteprednol Etabonate

- Site-specific steroids often referred to as “soft steroids”
- Two strengths, .5% (Lotemax) and .2% (Alrex)
- Both made by B & L

Lotemax

- Very unique agent! 0.5% Loteprednol
- Almost as potent as Pred Forte but very little propensity to elevate IOP or cause PSC’s
- In the eye, it binds to the target site and achieves therapeutic effect but then is quickly broken down
- Intrinsic esterases turn the drug into cortenic acid which is an inactive metabolite
- Available in ointment form which is preservative free and as a “gel” forming drop

Lotemax

- This allows for excellent therapeutic effect with a substantially reduced propensity to cause problems
- Penetrates very well
- Potent enough to be used for almost everything except acute iritis / iridocyclitis
- Often “the” choice for chronic intraocular inflammation
- Expensive, but drug program through Walgreens for $35 copay unless government insurance.

Alrex

- 0.2% Loteprednol
- Similar to Lotemax but not potent enough to treat intraocular inflammation
- Excellent for chronic treatment of allergies and dry eye
- Cost issues: can cost more than Lotemax

Dexamethasone

- Dexamethasone sodium phosphate or alcohol suspension
- 0.1% suspension (Maxidex)
- Potent, but tremendous ability to increase IOP
- Frequently used in combination with antibiotics (Tobradex, Maxitrol, Dexacidin)
- Tobradex ST: only 0.05% dexamethasone
Fluoromethalone

- Relatively weak, little risk of elevating IOP but limited clinical uses
- .1% ointment (FML)
- .1% suspension (FML and Eflone)
- .25% suspension (FML Forte)
- .1% acetate suspension (Flarex)

Rimexolone

- 1% suspension (Vexol)
- Claims to have less propensity to increase IOP, which is true, but it still does
- Limited clinical niche

Combinations

- Maxitrol, Dexacidin
- Pred-G
- Tobradex (has a generic) & Tobradex ST, Zylet
- Blephamide, Vasocidin
- FML-S

#3) Topical NSAIDS

Ketoralac

- Acular LS 0.4% (what does LS stand for?). QID
- Acuvail preservative free, unit dose vials. BID
- Original Acular was .5% and it had substantial issues with stinging
- Uses for topical NSAIDS include surface pain, post-operative pain / inflammation, CME, and occasionally allergic conjunctivitis

Voltaren

- Diclofenac .1%
- Generically available (earlier generic forms linked to corneal melting)
- QID dosing
**Nevanac**
- Nepafenac .1%
- Prodrug
- TID dosing
- Excellent for CME
- Expensive
- Newer Ilevro .3% Nepafenac
- QD dosing
- $250 for 1.7 ml

**Bromday**
- Bromfenac .09%
- Has a generic, but still $140 for 1.7ml
- QD dosing
- Also Prolensa .07%.
- Decreased PH to increase corneal penetration (1.6 ml and 3ml)
- Also new Bromsite .075%

**Not an NSAID, but.......**
- Restasis
- Topical cyclosporin A: Inhibits T-cells
- Emulsion
- Now in multi-dose bottle
- Takes weeks to months for maximum effect
- BID dosing, can sometimes decrease to QD after chronic use
- HSK? HZV? Atopic disease

**Another dry eye medication**
- Lifitegrast (Xiidra) 5%
- Shire pharmaceuticals
- FDA approval granted in July of 2016
- BID dosing for dry eye
- Not exactly clear how it helps in dry eye, but most likely blocks T-cell adhesion, thus limiting T-cell mediated inflammation.
- Works quicker than Restasis, within about 2 weeks
- $450.00 / 60 vial carton

**#4) Topical Anti-Allergy Medications**
- Ketotofin based mast cell / antihistamine combination products
- Old antihistamine / vasoconstrictor combos
- Vasocon-A, Naphcon-A

**The OTC players......**
- Alaway (most cost effective due to 10ml bottle) CVS has a generic
- Zaditor
- Caritin Eye
- Refresh Allergy
- All BID for a couple of weeks, then possibly QD chronically
Mast Cell Stabilizing / Antihistamine Combination Products

- QD dosing
- Pataday
- Lastacaft
- Pazeo

- BID dosing
- Bepreve (10 ml, may have positive effect on allergic rhinitis)
- Elestat (generic available)
- Optivar (also generic)
- Patanol (also generic)
- Zerviate (topical version of Zyrtec)

Newly approved agent

- Zerviate
- .24% Ceftirizine (Zyrtec)
- Nicox

Other agents

- Pure antihistamine
  - Emadine
  - QID dosing

- Pure mast cell stabilizers
  - Alamast
  - Alocril (BID)
  - Alomide
  - Crolom
  - Opticrom
  - Most are QID dosing

#5) Topical Antiviral Agents

Viroptic

- HSK Epithelial lesions respond extremely well to topical antiviral therapy. Historical mainstay of treatment is Viroptic (trifluridine).
- Extremely effective against HSV but very toxic to the cornea. Also, very expensive, even generic

Viroptic

- Viroptic is utilized Q 2-3h with an ideal maximum of around nine drops per day (toxicity). Once epithelium heals, decrease to QID for about 1 more week
- Medicamentosa is very common with secondary keratitis but the drug is almost universally effective in treating the infection
Another topical option is Zirgan, a gel forming drop. May also be effective against adenovirus. Prolonged contact time, so dosing is less: 5 times per day until the epithelium is intact, then TID for several more days. Unfortunately, extremely expensive.

Zirgan has been used in Europe under the name Virgan with a long track record. Possibly effective against adenovirus as well. Can work against Zoster dendrites as well (nothing else does).

Older agents that are no longer readily available include IDU (Idoxuridine) and Vira-A (vidaribine) ointment.

A viable alternative to topical therapy is the use of oral antiviral agents. Can be very effective, but may take a while longer to work. Very, very cost effective if using Acyclovir. Dosing is 800mg TID. Cost of around $30. Also available in 200mg pills on most $4 / $10 plans. Can run in to issues with supply (need 12 pills per day).
Prostaglandins

- Four drugs
- Xalatan and generic
- Travatan-Z / generic Travatan
- Lumigan and generic
- Zioptan

Prostaglandins

- Work by increasing uveoscleral outflow
- Under normal circumstances uveoscleral outflow in humans accounts for only 10-20% of drainage

Prostaglandins

- Very effective
- Can lower IOP 30% and more
- Can get remarkable effects with very high pressures
- First choice for many practitioners
- QD dosing: does not have to be QHS
- Synergistic with other topical meds
- Most synergistic with CAI’s and Alpha 2 agonists, seem to be least so with Beta blockers (studies vary)
- Relatively slow onset of action

Prostaglandin side effects

- Contraindicated to some degree in........
- Uveitic and Neovascular glaucoma
- History of uveitis
- History of HSK
- During cataract post-op

Prostaglandin side effects

- Can darken mixed colored irises
- Hyperpigmentation of eyelid skin
- Hypertrichosis
- Hyperemia
- “Orbitopathy”, ? Lid clicking
- Almost entirely free of significant systemic side effects

Xalatan

- Latanaprost .005%
- Generic is available
- Longest track record
- Seems to have the most propensity to change iris color
- Aphakia
- History of CME
- Mixed colored irises?
- Unilateral Treatment
- Not very helpful with acute angle closure (take too long to work)
Travatan-Z
• Travaprost .004%
• Preserved with Sofzia, so less toxicity
• Old original Travatan available generically

• Any blood testing indicated for the patient pictured here?

Lumigan
• Bimataprost .03% (old-generically available) and .01%
• May be slightly more potent than Xalatan and Travatan-Z
• Most prominent side effect profile
• If one does not work, try another?

Zioptan
• .0015% Tafluprost
• Preservative free
• FDA approval for OAG and ocular hypertension

Latanaprostene Bunod
• Approved by the FDA in late 2017
• Vyzulta
• Once per day dosing
• Unique agent that increases both uveoscleral outflow and TM outflow

Rhokinase inhibitors
• A completely novel drug class for glaucoma
• Rhopressa: approved by FDA in late 2017
• Roclatan: Rhopressa combined with Latanaprost: in clinical trials

• Increases TM outflow
• Lowers episcleral venous pressure so lowers outflow resistance
• Decreases aqueous production

Beta Blockers
• Many available
• Both .5% and .25%
• Many can be used QD: Can try .25% QAM in mild cases and work up from there
• Decrease aqueous production

• Very, very inexpensive in generic form
• Expect IOP drop of around 25%
• Dose in AM when using QD
Beta Blockers

- Timolol / Timoptic .25% and .5% ($4 / $10 plans)
- Betagan .25% and .5%
- Betimol .25% and .5%
- Istalol .5%
- Timoptic XE and Timoptic XE PF .25% and .5%
- Most available as generics

Beta Blocker contraindications / SE’s

- Well known with very long track record......
- Depression
- Impotence
- Effects on cholesterol levels
- Topical drops less effective when on oral beta blockers
- Very safe over all

Alpha -2 agonists

- Alphagan and Alphagan-P
- Confusing ! Alphagan .2%, Alphagan-P .15%, and Alphagan-P .10%
- .2% and Alphagan-P .15% generically available
- What does the “P” stand for? Purite (preservative in place of BAK)
- Combigan (.2% A and .5% T)
- Simbrinza (.2% A and Trusopt)

Alphagan (P)

- Dosed BID; rarely TID
- Expect IOP drop of around 20%
- Work by decreasing inflow and increasing TM outflow
- Now also Lumify (Brimonidine 0.025%) for OTC redness relief. Less chance of rebound hyperemia and tachyphylaxis, selectively constricts veins

Alphagan SE’s

- Dry mouth
- Hyperemia
- Follicular toxic conjunctivitis
- Fatigue!!!!!!!
- Can’t use with MAOI’s.......but who takes those? Nardil & Parnate

Topical CAI’s

- Two : Trusopt and Azopt
- Relatively safe but not very potent as monotherapy
- Expect IOP drop around 15-20%
- More synergistic with prostaglandins however
- Dosed BID , TID occasionally
- Cosopt is combo drop with Trusopt and Timolol .5%
- Trusopt and Cosopt have generics
- Simbrinza: Trusopt and .2% Alphagan combination. Dosed BID-TID. Horrible problem with follicular toxic response; Far more common than with .2% Alphagan alone
- Work by decreasing inflow
Topical CAI SE’s

- Burning and stinging (especially Trusopt)
- Sulfur allergies (but not a problem for some with systemic allergy)
- Can be hard on corneal endothelium: watch with Fuch’s
- Metallic taste

Glaucoma treatment during pregnancy and / or nursing

- Many things to consider
- Most important during first trimester due to organogenesis, then again during nursing
- IOP drops naturally during pregnancy

Pregnancy / Nursing

- Alphagan (pregnancy)
- Beta Blockers (both)
- Prostaglandins while nursing

Pregnancy / Nursing

- Alphagan the “safest” based upon category but can cause severe CNS depression and apnea in infants, so D/C shortly before birth
- Many practitioners feel the most safe using beta-blockers, because systemic B-blockers are used for HTN in pregnancy

Pregnancy / Nursing

- Avoid prostaglandins (used systemically to induce labor)
- Use NLDO or punctal plugs to minimize systemic absorption in all cases

#7) Oral Antibiotics and Oral Antivirals

- Pills that we prescribe to our patients

Summary: Alphagan or Beta Blocker during pregnancy
Prostaglandins or Beta Blockers during lactation
Oral Antibiotics: Ocular Indications

- Beat the bugs!
- Rosacea / Ocular Rosacea
- Dacryoadenitis
- Dacryocystitis
- Preseptal Cellulitis
- Hordeola / Chalazia
- Blowout Fractures

Cost

- $4 (30 day) and $10 (90 day) lists for generics at Kroger, Walmart, Target etc.
- Indicated by an * during talk
- Meijer has some generic antibiotics for free

Cephalexin *

- 250 or 500 mg (QID or BID)
- Excellent broad spectrum cephalosporin
- Bactericidal
- Cross sensitivity with penicillin regarding allergies but not with everyone
- Keflex brand = very expensive!
- Up to 60% resistance in facial cellulitis

Dicloxacillin

- Penicillinase resistant penicillin
- Great for soft tissue infections
- Bactericidal
- Nausea, allergies, diarrhea
- 250 mg QID or 500 mg BID

Augmentin

- Amoxicillin plus clavulanate: 250, 500mg TID or 875mg BID
- Works on bugs that are resistant to penicillin due to penicillinase
- Bactericidal, good coverage
- Allergies
- 500mg available generically

Tetracycline *

- 250 or 500 mg QID
- Bacteriostatic but much resistance
- Poor for soft tissue disease
- Can not be used in pregnant women or children due to effect on bone and enamel formation (discoloration of teeth)
- Makes BC Pill less effective
- Photosensitivity, stomach upset, calcium inactivation (take on empty stomach)
- Great lipid / acid modulating effects
**Doxycycline**
- 50 or 100 mg BID
- Periostat: 20 mg
- In tetracycline family
- Can take with food
- Less problems with photosensitivity
- Still get stomach upset
- As effective as tetracycline but fewer side effects, better dosing.
- Cost has gone way up
- Oracea (30 /10 )
- Usefull in RCE management
- Minocycline: 50 or 100 mg BID. Long term use can cause blue / black discoloration of skin, nails, and sclera

**Azithromycin**
- Zithromax Z-pack: 6, 250 mg capsules. Is a macrolide. Moderate price. Can also dose 1 gram, one time
- Take 500 mg (2) the first day and one 250 mg tablet each of the next 4 days with Z-pack
- May enhance the effect of oral anticoagulants
- Works like doxy family with rosacea / MGD / chalazia
- 2 X risk of sudden cardiac death in heart patients

**Azithromycin**
- Now has FDA warning for fatal arrhythmia
- Greater risk if prolonged QT interval, bradycardia, hypomagnesia
- Many experts calling for ban due to resistance concerns. Long half life and broad spectrum contribute majorly to overall resistance.

**Bactrim**
- Trimethoprim and Sulfamethoxazole: one tablet contains 80 mg T and 400 mg S (also available in double strength). One double-strength tablet Q12h
- Can not use if patient has sulfa allergy
- Excellent against MRSA, toxoplasmosis

**Ciprofloxacin**
- Fluoroquinolone: 750 / 500 / 250 BID
- 5mg/100ml suspension
- Effective but overused so resistance an issue. Lavaquin shows less resistance
- Can not use in patients under 18 due to joint tendon problems
- Possible increased risk of RD? 3% vs. .6% in one study. Follow up studies conflict
- Possible increased uveitis risk (2X)

**Oral Fluoroquinolones**
- Significant side effects......
- Peripheral neuropathy
- Tendon rupture
- Heart arrhythmia
- Dysglycemia in diabetics
Oral Antivirals

- Used to manage Herpes Simplex and Herpes Zoster

Oral Antivirals-Dosing Simplex

- Acyclovir (200,400,800): 200mg QID/ 400BID; up to 800mg TID
- Also available in a pediatric suspension
- Only 200mg on $4 / $10 plans

- Famvir (125,250,500)
  - 500mg TID

- Valtrex 500mg
  - 500 mg TID
  - Better bioavailability than Acyclovir

Oral Antivirals-Dosing Zoster

- Acyclovir: 800mg 5X day for 10 days
- Famvir: 500mg TID x 1week
- Valtrex: 1000 mg TID X 1 week

Side Effects of Antivirals

- Very safe
- Caution with renal impairment
- Headache
- GI upset / abdominal pain

Hutchison’s sign with Zoster

Zoster vaccine

- Live vaccine
- Zostavax
- Approved by US FDA for immunocompetent patients 50 and up
- CDC recommends for age 60 and up
- 1 in 3 persons in US will develop zoster

Zoster vaccine

- Can not use if history of severe allergic response to Neomycin or gelatin
- Must be off oral antivirals for one day before and two weeks after the vaccine
- Reports of reactivation of ocular HZ disease after the vaccination
- May decrease the severity of PHN

Zoster vaccine
Zoster vaccine

- Effect may wane after about 8 years or so, may last longer in younger patients
- Only 24% of eligible US adults over 60 have received it
- Rate of zoster decreased by 68% in 50-59 year olds, 63.9% in 60-69 year olds, and 37.6% in those 70 and older
- Is the increase in adult zoster cases due to chicken pox vaccination for kids?

Newly approved Zoster Vaccine

- Shingrix
- One shot, followed by a second shot 2-6 months later
- Just starting to become available in late 2017
- Recommended for age 50 and up
- Believed to be about 90% effective
- More pain, more malaise

Ocular Side Effects of Oral Medications

- Pills that other doctors prescribe that affect the eye
- Plaquenil
  - Hydroxychloroquine
  - One of the most common reasons for routine ocular screening for adverse reaction
  - Used mostly for treatment of RA and Lupus, other emerging uses
  - About 150,000 people in the US
- Chloroquine (Aralen)
  - Used as an antimalarial drug; very rarely for RA/Lupus
  - Much greater chance of ocular damage
  - Rare to be on long term therapy

Plaquenil

- Dose is 200mg or 400mg daily. 400mg common
- Prescribed in 200 mg tablets
- Occasionally see 300 mg per day used (cut pills in half)
- Increased risks of ocular damage include:
  - Daily dose over 5.0 mg/kg/day using strictly actual weight (old standard for many years was 6.5 mg/kg/day using ideal body weight)
  - Renal dysfunction
  - Other maculopathy
  - Tamoxifen use concurrently (5 X risk)
- If patients are on 200mg / day ocular problems are very rare
- At 400mg / day for extended periods of time the risk is much greater
- Ocular damage and symptoms can progress after meds have been D/C
- Damage can be irreversible
Plaquenil

- Affects the photoreceptors and then the RPE
- Stores in Melanotic tissue, the liver, and the kidney
- Excreted mostly by the kidney
- Damage begins in a ring around the center of the fovea

Chance for retinal toxicity

- At doses below the 5.0 mg/kg/day threshold
  - < 1% risk at 5 years
  - < 2% risk at 10 years
  - 20% risk at 20 years

- Marmor and Melles 2014: study of 2361 patients with use over 5 years: 177 with toxicity (7.5%): all doses included

Ocular side effects of Plaquenil

- Bulls eye pigmentary maculopathy: late!
- Visual field loss
- Decreased vision and contrast sensitivity
- Color vision changes
- Vortex keratopathy (rare......more common with chloroquine)

Plaquenil management

- Testing should include..............
- Baseline exam with fundus evaluation within one year of beginning medications
- Management guidelines updated June 2016

Looking for pre-existing pathology

Supplementary diagnostic tests not needed at baseline visit

Plaquenil managment

- Then after five years of use......
- Yearly exams with 10-2 VF (white on white) and SD-OCT
- Also can consider FAF and multifocal ERG as extra testing
- See more frequently and before five years if extensive risk factors present or dose above threshold

VF defects with Plaquenil

- HVF 10-2 white on white
- Use pattern deviation plot
- Look for paracentral ring scotoma or partial ring scotoma in area 2-6 degrees from center
- Take any defect, even modest defects of 4-8 DB, seriously
Plaquenil management

- Multifocal ERG (very sensitive, but extremely variable: should not be used alone), SD-OCT (Flying Saucer sign), FAF.
- Report to rheumatologist
- Assess for dose toxicity at every visit
- We have the ability to detect toxicity before vision loss occurs and before fundus changes are visible

Chen et al. Clinical Ophthalmology 2010:4 p. 1151

- Recent study in Ophthalmology (January 2014 online) showed........
- Out of 150 individuals showing clear toxicity after cumulative dose of over 1000g........
- 90% showed defects on both 10-2 VF and OCT
- 10% showed VF defect, but no OCT defect. Zero with OCT but no VF

Late progression

- Marmor and Hu JAMA online June 2014
- 11 patients with toxicity
- Followed for three years after D/C Plaquenil
- Categorized as mild / moderate / severe toxicity
- Mild / moderate showed no progression after D/C
- Severe progressed for up to three years

Late progression

- Basically no progression of VA or VF loss
- Significant progression in severe cases of SD-OCT and FAF damage
- May be related to eventual death of already critically damaged RPE cells and foveal cones
- Plaquenil found in blood in low amounts one year after D/C
Bull’s Eye Maculopathy

- 5 cases of Bull’s Eye Maculopathy reported with Sertraline (Zoloft)
- An SSI used for depression
- Very rare, but very significant

One case involved a 14 year old whose vision dropped to 20/200 in each eye after one year of use. Did not recover or improve after three years off of the drug

Chloroquine maculopathy

Critical caveat

- In Asian patients, damage tends to be paramacular and can extend out to the arcades
- More diffuse maculopathy instead of a bullseye pattern
- Must perform 24-2 or 30-2 VF instead of a 10-2 because damage tends to be further out
- SD-OCT scans need to be performed outside of the fovea too
- FAF a good choice
Pegylated Interferons

- Treatment used mainly for hepatitis.
- Very long treatment course
- Can cause retinal CWS and other vascular retinopathy / macular edema
- Can be sight threatening but rarely are
- Most common is CWS near the optic nerve
Interferons

- Inform prescribing physician
- Endogenous interferon levels rise with cancer so.................
- Watch for isolated CWS with no explanation......think undiagnosed cancer! Also remember HIV and GCA

CWS secondary to interferons

Flomax

- Prostate therapy (Alpha 1 blocker)
- Also affects iris dilator muscle
- IFIS (Intraoperative Floppy Iris Syndrome)
- Leads to progressive miosis with floppy iris during intraocular surgery. Makes cataract surgery quite challenging!

Flomax

- Stopping the medicine before surgery does not appear to be effective
- Occurs to a much lesser degree with Hytrin, Cardura, and Uroxatrol.

Rapaflo

- Newer medication (silodosin) for BPH that is also highly selective for Alpha 1A receptors
- Same risk for IFIS as Flomax

Phenothiazines

Phenothiazines – Chlorpromazine (Thorazine), Thioridazine (Mellaril)

Older antipsychotic agents

- Decreased accommodation
- Dry eye
- ASC cataracts
- Corneal endothelial pigment deposits
- Macular pigment changes (mostly chlorpromazine)
Phenothiazines

- Macular pigment changes are sight threatening, cornea and lens changes have little impact on vision
- Other more common meds like Prozac and Zoloft affect accom.

Amiodarone

- Antiarrhythmic agent (K+ channel blocker)
- Cardarone or Pacerone
- Half life of up to 100 days!
- Vortex keratopathy
- Almost universal after six months or more of therapy
- Does not typically have a major impact on vision but can
- Resolves months after therapy is discontinued
- Can also rarely affect color vision
- Fabry's Disease (X-linked; lipid storage disorder caused by enzyme deficiency)
- Limbal stem cell deficiency

Amiodarone

- Also causes bilateral optic nerve head edema in 2% of patients
- Mimics NAION but occurs in both eyes
- VA changes slowly recover and often return to baseline norms after discontinuing the drug but VF changes may not

Amiodarone

- Nerve swelling

Digoxin

- Cardiac agent used for atrial fibulation / flutter and CHF
- If doses exceed standard therapeutic levels, 95% of patients develop ocular complications
**Digoxin**

- The most common ocular side effect is color disturbance.....often taking the form of a gold or yellow tinge to images
- Haloes and other color changes are possible

**Dilantin (Phenytoin)**

- Anticonvulsant
- Used to treat seizures / epilepsy
- Ocular side effects include blue-yellow color disturbance, nystagmus, diplopia, and rarely ophthalmoplegia
- Nystagmus and color disturbances are relatively common and are dose related

**Topamax (Topirimate)**

- Anticonvulsant used for migraines, epilepsy, depression, bipolar disease and weight loss
- Carries FDA warning for ocular side effects
- Many cases of acute, bilateral angle closure

**Digoxin**

- Rare ocular side effects include..........
- Optic neuritis
- Loss of central vision
- Decreased acuity

**Dilantin**

- Standard eye exam with addition of blue / yellow color testing
- Report problems to the patient’s neurologist

**Topamax**

- Severe edema of the ciliary body leads to angle closure, excessive myopic shift and even uveal effusion
- Occurs most often within 2 weeks
**Topamax**
- Can also happen with other sulfonamides but very rare.
- Hydrochlorothiazide
- Diamox
- Sulfasalazine
- One case reported with Wellbutrin, Tamiflu

**Fosamax**
- Biphosphonate
- Used to treat osteoporosis, rarely Paget’s disease and bone metastases

**Tamoxifen (Nalvodex)**
- Antiestrogen therapy for the management of breast cancer
- Similar in chemical structure to chloroquine
- 6% get ocular side effects
- Causes a crystalline retinopathy

**Fosamax**
- Ocular side effects include:
  - Scleritis!
  - Iritis
  - Conjunctivitis
  - Ptosis
  - Yellow color disturbance
  - Diplopia

**Tamoxifen retinopathy**
- Can cause:
  - Vortex keratopathy
  - Macular edema with decreased vision
  - Leads to decreased optic cup volume secondary to astrocyte swelling
  - Report to oncologist/physician
  - Monitor yearly
  - May see more now that guidelines recommend 10 year Tx instead of 5 years
Talc retinopathy

Canthaxanthine

Tanning agent

Ethambutol

- TB treatment
- Can cause optic neuropathy with severe and lasting vision loss
- 1% chance
- In use since 1960
- Isononiazid now favored for treatment, but also linked to optic neuropathy
- Central or ceco-central VF loss but......
- Also has the ability to damage the chiasm and lead to bi-temporal VF loss

Isoretinoine (Accutane)

- Used to treat Acne
- Ocular side effects include......
- Dry eyes / meibomian gland dysfunction
- Conjunctivitis
- Decreased night vision

Accutane

- Rare ocular side effects include corneal deposits, color vision disturbances, acute myopic shifts, and increased ICP leading to papilledema

Viagra / Levitra / Cialis

- Phosphodiesterase 5 inhibitors
- Prescribed for ED
Viagra etc.

- Works on PDE 5, but PDE 6 is found in the retina and the drugs have some effect on it (10 X more effect on PDE 5)
- Changes in color perception are common, many colors possible
- Increased light sensitivity, photopsia
- Dose dependent: those taking 200mg of Viagra have 50% chance of ocular side effects; 50 mg <5 % (normal dose)

Viagra / Cialis / Levitra and NAION

- 553 cases officially reported to the FDA by the end of 2014. 443 were Viagra
- ? Under reported
- These medications also occasionally used for pulmonary HTN
- Visual loss most often noted upon awakening the morning after use
- Is the association real or coincidence?
- Likely the “straw that broke the camel’s back” in those with risk factors. But.................

ED drugs and NAION

- Very interestingly, has been reported in a 7 month-old infant, 28 year old, and 33 year old, presumably all taking them for pulmonary HTN
- At those young ages, not as likely to have other NAION risk factors
- 2 reported cases of PION, one in a female with use for pulmonary HTN

Viagra / Cialis

- What is the proposed mechanism? Nitrous oxide release actually dilates vessels…..but drops blood pressure.
- Do ION patients have faulty autoregulation?
- Ask all males with NAION about ED drug use. D/C if using to protect fellow eye.

The end!